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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	PAPER NUMBER
1624	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,702	GE ET AL.	
	Examiner	Art Unit	
	Brenda L. Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/13/2006 & 12/9/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-31 are pending in the application.

Election/Restrictions

1. Applicant's election with traverse of Group II in the reply filed on December 9, 2008 is acknowledged. The traversal is on the ground(s) that the compounds with the 7 and 8-membered rings and X as defined are closely related to one another structurally when considered as part of the larger ring system in Claim 1, and they also have the same therapeutic activity. The applicants indicated that reconsideration of the restriction requirement combining Groups I and II would not be traversed. Upon further consideration Groups I and II will be combined, thus the claims have been examined such that X is C and the size of the rings are 7 and 8 membered rings.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 29 and 30 are rejected under 35 U.S.C. 1 12, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In evaluating the enablement question, several factors are to be considered. In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988)., Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount

of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The scope of the method claims are not adequately enabled solely based on the inhibition of the chemokine receptor CC, CCR5 or CCR2 provided in the specification. Instant claim language embraces disorders not only for treatment, but, for prevention which is not remotely enabled. It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop inflammatory, immunoregulatory disorder or disease. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein. Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied upon are reasonably predictive of in vivo efficacy by those skilled in the art. See In re Ruskin, 148 USPQ 221., Ex parte Jovanovics, 211 USPQ 907., MPEP 2164.05(a). Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. Genentech Inc. v. Novo Nordisk 42 USPQZd 1001.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the moiety -$NR^{12}SO_2NR^{12}R^{12}$-, which contains a hyphen after $NR^{12}R^{12}$.

b. Claim 1 recites the limitation "cycloalkyls" in the definition of the substituents within R^1. There is insufficient antecedent basis for this limitation in the claim.

c. Claims 1, 6 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the second occurrence of -O-C_{1-3}alkyl in the definition of the substituents on the alkyls and cycloalkyl[s] of R^1.

d. Claim 6 recites the limitation "1-7 substituents" in the definition of the substituents on the heterocycle within R^1. There is insufficient antecedent basis for this limitation in the claim.

e. Claim 6 recites the limitation "-COR^{11}, -CN, -$NR^{12}R^{12}$, -$CONR^{12}R^{12}$, and -$NCOR^{13}$" in the definition of the substituents on the heterocycle within R^1. There is insufficient antecedent basis for this limitation in the claim.

f. Claim 6 recites the limitation "-$NR^{12}R^{12}$, -$CONR^{12}R^{12}$, and -$NCOR^{13}$" in the definition of the substituents on the alkyl and cycloalkyl within R^1. There is insufficient antecedent basis for this limitation in the claim.

g. Claims 6 and 7 are vague and indefinite in that it is not known what is meant by the moiety -$NCOR^{13}$, which is not valence satisfied on the N atom.

h. Claim 7 recites the limitation "-NCOR^{13} or -NR^{12}R^{12a}" in the definition of the substituents on the heterocycle within R^{1}. There is insufficient antecedent basis for this limitation in the claim.

i. Claim 8 recites the limitation "-NHCOR^{13a}" in the definition of the substituents on the thiazole within R^{1}. There is insufficient antecedent basis for this limitation in the claim.

j. Claim 9 recites the limitation "-NHCOCH$_3$ at the 2 position of the thiazole ring" in the definition of the substituents on the thiazole ring within R^{1}. There is insufficient antecedent basis for this limitation in the claim.

k. Claim 13 is vague and indefinite in that it is not known what is meant by "antrifluoromethyl".

l. Claim 19 recites the limitation "-COR^{11}, -CN, heterocycle and -CONR^{12}R^{12a}" in the definition of the substituents on the C$_{1-6}$alkyl within R^{7}. There is insufficient antecedent basis for this limitation in the claim.

m. Claim 21 is vague and indefinite in that it is not known what is meant by the comma at the end of the claim.

n. Claim 22 recites the limitation "-F" in the definition of R^{8}. There is insufficient antecedent basis for this limitation in the claim.

o. Claim 24 is vague and indefinite in that it is not known what is meant by "whereinR^{7}".

p. Claim 29 is vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in

determining which are the diseases capable of being mediated by a chemokine receptor. It is unclear which diseases are associated with each of the chemokine receptors. Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties in vitro, when administered to a patient with a certain disease, does not produce a favorable response. One cannot conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital -- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration cannot be predicted in advance. Should our drug be given as a bolus iv or in a time release po formulation. Thus, how many dosages and

dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active in vitro, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of which are inhibitors in vitro, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the accurate answer, and that the success of second compound arises from some other unknown property, which the second drug is capable. It is common for a drug, particularly in cancer and CNS diseases, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation shown to affect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy, which are not themselves effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the ad cannot determine the actual scope of the claim. Hence, the claim is indefinite.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-31 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims1, 7, 8, 10-22, 24-

27, 35-37 and 39-44 of copending Application No. 10/567,516. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds, compositions and method of use of the compounds of formula I of the instant invention are embraced by the compounds, compositions and method of use of the compounds of formula II of 10/567,516 where X is C.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. Claims 1-6 and 8-31 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 7, 8, 11-20, 22, 26 and 27 of copending Application No. 10/533,337. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds, compositions and method of use of the compounds of formula I of the instant invention are embraced by the compounds, compositions and method of use of the compounds of formula II of 10/567,516 where X is C.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brenda L. Coleman/
Primary Examiner, Art Unit 1624